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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HUYNH, PHUONG N	
ART UNIT	PAPER NUMBER
1644	
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10/25/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/596,012	SANDBERG ET AL.	
	Examiner	Art Unit	
	PHUONG HUYNH	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *One* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 June 2008*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,5,7-10,12-14,18,21,26-28,30-34,38,39 and 42-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *See Continuation Sheet* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims subject to restriction and/or election requirement are 1-2, 4, 5, 7-10, 12-14, 18, 21, 26-28, 30-34, 38-39 and 42-45.

DETAILED ACTION

Claims 1-2, 4, 5, 7-10, 12-14, 18, 21, 26-28, 30-34, 38-39 and 42-45 are pending.

REQUIREMENT FOR UNITY OF INVENTION

As provided in 37 CFR 1.475(a), a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ("requirement of unity of invention"). Where a group of inventions is claimed in a national stage application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

The determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim. See 37 CFR 1.475(c).

When Claims Are Directed to Multiple Categories of Inventions:

As provided in 37 CFR 1.475(b), a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories:

(1)A product and a process specially adapted for the manufacture of said product; or

(2)A product and process of use of said product; or

(3)A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or

(4)A process and an apparatus or means specifically designed for carrying out the said process; or

(5)A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.

Otherwise, unity of invention might not be present. See 37 CFR 1.475(c).

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

I. Claims 2, 4-5, 7-10, 12-14, 18, 21, 26-28 and 30-32, drawn to a conjugate comprising a) a trifunctional cross-linking moiety, to which is coupled b) an affinity ligand via a linker 1, c) a cytotoxic agent, optionally via a linker 2, and d) an anti Erb antibody or variants thereof having the ability to bind to Erb antigens expressed on mammalian tumor surfaces with an affinity-binding constant of at least $5x10^6$ M^{-1}, wherein the affinity ligand is biotin, or a biotin derivative having essentially the same binding function to avidin or streptavidin as biotin, wherein stability towards enzymatic cleavage of the biotinamide bond has been introduced in linker 1, the **anti-Erb antibody or variants thereof are direct to Erb1**, a composition and kit comprising said conjugated.

II. Claims 2, 4-5, 7-10, 12-14, 18, 21, 26-28 and 30-32, drawn to a conjugate comprising a) a trifunctional cross-linking moiety, to which is coupled b) an affinity ligand via a linker 1, c) a cytotoxic agent, optionally via a linker 2, and d) an anti Erb antibody or variants thereof having the ability to bind to Erb antigens expressed on mammalian tumor surfaces with an affinity-binding constant of at least $5x10^6$ M^{-1}, wherein the affinity ligand is biotin, or a biotin derivative having essentially the same binding function to avidin or streptavidin as biotin, wherein stability towards enzymatic cleavage of the biotinamide bond has been introduced in linker 1, the **anti-Erb antibody or variants thereof are direct to Erb2**, a composition and kit comprising said conjugate.

III. Claims 2, 4-5, 7-10, 12-14, 18, 21, 26-28 and 30-32, drawn to A conjugate comprising a) a trifunctional cross-linking moiety, to which is coupled b) an affinity ligand via a linker 1, c) a cytotoxic agent, optionally via a linker 2, and d) an anti Erb antibody or variants thereof having the ability to bind to Erb antigens expressed on mammalian tumor surfaces with an affinity-binding constant of at least $5x10^6$ M^{-1}, wherein the affinity ligand is biotin, or a biotin derivative having essentially the same binding function to avidin or streptavidin as biotin, wherein stability towards enzymatic cleavage of the biotinamide bond has been introduced in linker 1, the **anti-Erb antibody or variants thereof are direct to Erb3**, a composition and kit comprising said conjugate.

IV. Claims 2, 4-5, 7-10, 12-14, 18, 21, 26-28 and 30-32, drawn to A conjugate comprising a) a trifunctional cross-linking moiety, to which is coupled b) an affinity ligand via a linker 1,

c) a cytotoxic agent, optionally via a linker 2, and d) an anti Erb antibody or variants thereof having the ability to bind to Erb antigens expressed on mammalian tumor surfaces with an affinity-binding constant of at least $5x10^6$ M^{-1}, wherein the affinity ligand is biotin, or a biotin derivative having essentially the same binding function to avidin or streptavidin as biotin, wherein stability towards enzymatic cleavage of the biotinamide bond has been introduced in linker 1, the **anti-Erb antibody or variants thereof are direct to Erb4**, a composition and kit comprising said conjugate.

V. Claims 2, 4-5, 7-10, 12-14, 18, 21, 26-28 and 30-32, drawn to A conjugate comprising a) a trifunctional cross-linking moiety, to which is coupled b) an affinity ligand via a linker 1, c) a cytotoxic agent, optionally via a linker 2, and d) an anti Erb antibody or variants thereof having the ability to bind to Erb antigens expressed on mammalian tumor surfaces with an affinity-binding constant of at least $5x10^6$ M^{-1}, wherein the affinity ligand is biotin, or a biotin derivative having essentially the same binding function to avidin or streptavidin as biotin, wherein stability towards enzymatic cleavage of the biotinamide bond has been introduced in linker 1, the **anti-Erb antibody or variants thereof are direct to a specific combination of Erb1, Erb2, erbB3 and ErbB4**, a composition and kit comprising said conjugate.

VI. Claims 33-34, 38-39 and 42-45, drawn to a method for treatment and diagnosing of cancer expressing Erb gene products on the surface of its tumor cells in a mammalian host, wherein a medical composition comprising a conjugate comprising a) a trifunctional cross-linking moiety, to which is coupled b) an affinity ligand via a linker 1, c) a cytotoxic agent, optionally via a linker 2, and d) an anti Erb antibody or variants thereof having the ability to bind to Erb antigens expressed on mammalian tumor surfaces with an affinity-binding constant of at least $5x10^6$ M^{-1}, wherein the affinity ligand is biotin, or a biotin derivative having essentially the same binding function to avidin or streptavidin as biotin, wherein stability towards enzymatic cleavage of the biotinamide bond has been introduced in linker 1, the **anti-Erb antibody or variants thereof are direct to Erb1 is administered to the mammalian in need thereof.**

VII. Claims 33-34, 38-39 and 42-45, drawn to a method for treatment and diagnosing of cancer expressing Erb gene products on the surface of its tumor cells in a mammalian host, wherein a medical composition comprising a conjugate comprising a) a trifunctional cross-linking moiety,

to which is coupled b) an affinity ligand via a linker 1, c) a cytotoxic agent, optionally via a linker 2, and d) an anti Erb antibody or variants thereof having the ability to bind to Erb antigens expressed on mammalian tumor surfaces with an affinity-binding constant of at least $5x10^6$ M^{-1}, wherein the affinity ligand is biotin, or a biotin derivative having essentially the same binding function to avidin or streptavidin as biotin, wherein stability towards enzymatic cleavage of the biotinamide bond has been introduced in linker 1, the **anti-Erb antibody or variants thereof are direct to Erb2 is administered to the mammalian in need thereof.**

VIII. Claims 33-34, 38-39 and 42-45, drawn to a method for treatment and diagnosing of cancer expressing Erb gene products on the surface of its tumor cells in a mammalian host, wherein a medical composition comprising a conjugate comprising a) a trifunctional cross-linking moicty, to which is coupled b) an affinity ligand via a linker 1, c) a cytotoxic agent, optionally via a linker 2, and d) an anti Erb antibody or variants thereof having the ability to bind to Erb antigens expressed on mammalian tumor surfaces with an affinity-binding constant of at least $5x10^6$ M^{-1}, wherein the affinity ligand is biotin, or a biotin derivative having essentially the same binding function to avidin or streptavidin as biotin, wherein stability towards enzymatic cleavage of the biotinamide bond has been introduced in linker 1, the **anti-Erb antibody or variants thereof are direct to Erb3 is administered to the mammalian in need thereof.**

IX. Claims 33-34, 38-39 and 42-45, drawn to a method for treatment and diagnosing of cancer expressing Erb gene products on the surface of its tumor cells in a mammalian host, wherein a medical composition comprising a conjugate comprising a) a trifunctional cross-linking moicty, to which is coupled b) an affinity ligand via a linker 1, c) a cytotoxic agent, optionally via a linker 2, and d) an anti Erb antibody or variants thereof having the ability to bind to Erb antigens expressed on mammalian tumor surfaces with an affinity-binding constant of at least $5x10^6$ M^{-1}, wherein the affinity ligand is biotin, or a biotin derivative having essentially the same binding function to avidin or streptavidin as biotin, wherein stability towards enzymatic cleavage of the biotinamide bond has been introduced in linker 1, the **anti-Erb antibody or variants thereof are direct to Erb4 is administered to the mammalian in need thereof.**

X. Claims 33-34, 38-39 and 42-45, drawn to a method for treatment and diagnosing of cancer expressing Erb gene products on the surface of its tumor cells in a mammalian host, wherein a

medical composition comprising a conjugate comprising a) a trifunctional cross-linking moiety, to which is coupled b) an affinity ligand via a linker 1, c) a cytotoxic agent, optionally via a linker 2, and d) an anti Erb antibody or variants thereof having the ability to bind to Erb antigens expressed on mammalian tumor surfaces with an affinity-binding constant of at least $5x10^6$ M^{-1}, wherein the affinity ligand is biotin, or a biotin derivative having essentially the same binding function to avidin or streptavidin as biotin, wherein stability towards enzymatic cleavage of the biotinamide bond has been introduced in linker 1, the **anti-Erb antibody or variants thereof are direct to a specific combination of Erb1, Erb2, Erb3 and Erb4 is administered to the mammalian in need thereof.**

Linking claim 1 will be examined along with Groups I, II, III, IV or V if any one of said Groups is elected.

Claim 1 links inventions I-V. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim, claim 1. Upon the allowance of the linking claim, the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

The Groups of inventions listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Groups I-X lack unity of invention because the groups do not share same or corresponding technical feature.

Groups I-X lack unity of invention because even though the inventions of these groups require the technical feature of a conjugate comprising a) a trifunctional cross-linking moiety, to which is coupled b) an affinity ligand biotin or biotin derivative via a linker 1, c) a cytotoxic agent, optionally via a linker

2, and d) an anti Erb antibody or variants thereof having the ability to bind to Erb antigens expressed on mammalian tumor surfaces with an affinity-binding constant of at least 5x106 M-1, wherein the affinity ligand is biotin, or a biotin derivative having essentially the same binding function to avidin or streptavidin as biotin, wherein stability towards enzymatic cleavage of the biotinamide bond has been introduced in linker 1, this technical feature is not a special technical feature as it does not make a contribution over the prior art WO 00/02050 publication (PTO 1449) in view of WO 99/55367 or WO 01/00244 publication (PTO 144).

The WO 00/02050 publication teaches a conjugate comprising a trifunctional cross-linking moiety which coupled to an affinity ligand such as biotin via linker 1 (see abstract, pages 9-10), an effector agent such as diagnostic agent radionuclide or therapeutic agent such as toxin or enzyme (see page 10, lines 1-8, page 11, lines 19-27, page 12, in particular) and a targeting moiety or biomolecule reactive moiety such as tumor binding antibody (see page 6, line 22-25, in particular). The linker 1 which is to attach the biotin moiety to the trifunctional cross-linking moiety is chosen so that enzymatic cleavage of biotinamide bond has been introduced in linker 1 (see page 15-16, in particular). It may also impart increased water solubility and biotinidase stabilization (see page10, lines 19-26). The linker may contain hydrogen bonding atoms such as ethers or thioethers, or ionizable groups such as carboxylates, sulfonates, or ammonium groups, to aid in water solubilization of the biotin moiety (see page 15, lines 12-22 and claims 9-10). This conjugate is useful for column extracorporeal immunoabsorptive removal of a radiolabeled antibody conjugate from a patient's blood (see page 5, lines 25-35) as the affinity ligand (biotin) is non-bound.

The claimed invention in claim 1 differs from the teachings of the WO 00/02050 publication only in that the antibody is an anti-ErbB antibody with an affinity-binding constant of at least 5 x 10^{6}-M-^{1} instead of any monoclonal antibody that binds to tumor surface.

The WO 99/55367 publication teaches conjugate comprising Erb2 antibody conjugated to cytotoxin, or radionuclide (see claim 34-35, I particular). The reference Erb2 antibody binds to cancer cells with high affinity such as Kd x 10^{-9}M, which is at least 5 x 10^{6}-M-^{1} (see page 61, Table 3, in particular.

The WO 01/00244 publication teaches various Erb antibodies such as HERCEPTIN or erb2 antibody conjugated to toxin maytansinoid DM1 (see entire document, page 4, page 4, line 20, page 10, lines 10-12 in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made with reasonable expectation of success to substitute the monoclonal antibody in the conjugate of the WO 00/02050 publication for any Erb antibodies with high affinity as taught by the WO 99/55367 publication or WO 01/00244 publication as a suitable targeting molecule which has optimal binding to tumor surface.

Because Applicant's inventions do not contribute a special technical feature when viewed over the prior art, the inventions lack unity of invention.

Accordingly, Groups I-X are not so linked as to form a single general inventive concept and restriction is proper.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh, Ph.D. whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Thursday from 9:00 a.m. to 6:30 p.m. and alternate Friday from 9: 00 a.m. to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The IFW official Fax number is (571) 273-8300.

Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Phuong Huynh/
Primary Examiner, Art Unit 1644
October 22, 2010